

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

K2326-PCT

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/BE2004/000121

International filing date (day/month/year)
25.08.2004

Priority date (day/month/year)
26.08.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/14

Applicant
K.U. LEUVEN RESEARCH & DEVELOPMENT

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

response { $26.8.03 + 22m = 26.6.05$
 $04.1.05 + 3m = 04.4.05$ }

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 86.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/BE2004/000121

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/BE2004/000121

Box No. II Priority

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
4. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2-26,28-32
	No: Claims	1,27,33
Inventive step (IS)	Yes: Claims	
	No: Claims	1-33
Industrial applicability (IA)	Yes: Claims	1-33
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Re Item V.

The following documents have been cited in the search report. Where reference is made to them, the following numbering is used; unless otherwise indicated, reference is made to the relevant passages indicated in the Search Report:

- D1 : DATABASE WPI Section EI, Week 197930 Derwent Publications Ltd., London, GB; Class S02, AN 1979-G4608B XP002311257 & SU 627 334 A (FERMENT PRODUCT RES) 21 August 1978.
- D2 : US 4 676 439 A (HIRAI AKIRA ET AL) 30 June 1987 (1987-06-30)
- D3 : PATENT ABSTRACTS OF JAPAN vol. 2002, no. 04, 4 August 2002 (2002-08-04) & JP 2001 348581 A (SAWADA SHIGEMI; KOMATSU LTD), 18 December 2001 (2001-12-18)
- D4 : DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KUZNETSOV, YU. N. ET AL: "Electromagnetic grinding of materials" XP002311255 retrieved from STN Database accession no. 1977:75083.
- D5 : DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1987, SVALOV, S. A. ET AL: "Use of the magneto - induction effect for intensification of grinding" XP002311256 retrieved from STN Database accession no. 1987:481485.

Novelty (Art.33(2) PCT)

D1 discloses a method for milling powders to decrease the particle size where the powder is suspended in a magnetic field. The powder can be a chemical, a food or a medicinal preparation. Even if this document does not mention the degree of particle reduction, it is reasonable to expect that a decrease of the size of at least 25% will occur. In view of this prior art, the subject matter of claims 1, 27, 33 is not new in the sense of Art.33(2).

Furthermore, despite its wording, claim 33 is to be seen as a product by process claim, and is directed to a population of biologically active compounds "obtainable" using the process of claims 1 and 27. Since the milling method of the invention does not appear to produce a product which is different from the products of the prior art, this claim is not novel over any prior art composition comprising particles obtained using any other milling method.

Inventive step (Art.33(3) PCT)

The problem underlying the present invention is the provision of a process to reduce the dimension of particles (and agglomerates) of biologically active agents. Documents D2-D5 disclose milling processes to decrease the particle size of

powders, where the particles are suspended in a fluid (air), in a magnet field. These documents do not explicitly refer to the milling of biological active agents; however, it is clear that such processes are not restricted to a specific type of powder. The teaching of these documents would therefore prompt a skilled person confronted with the aforementioned problem, to apply the same milling techniques to decrease the size of particles of any biologically active compound, as claimed in the present application. In view of this prior art, the subject matter of claims 1, 27 and 33 do not appear to involve an inventive step.

The subject matter of the dependent claims is not characterized by any additional technical feature providing any new surprising technical effect over the prior art. For this reason, these dependent claims may also not be considered to involve an inventive step in the sense of Art.33(3) PCT.

Industrial Application

The subject matter of claims 1-33 is industrially applicable.

Re Item VI.

WO03072659 and WO2004043580, published after the priority date, but before the filing date, could become relevant if the priority of the present application will turn out not to be valid, and could become relevant in the proceedings before the national authorities of the designated states.